An Effective Method for the Oxidation of Aminofurazans to Nitrofurazans

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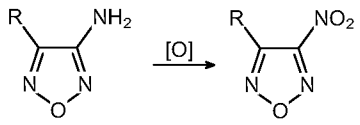
An effective method for the synthesis of nitrofurazans (NF) from aminofurazans (AF) has been developed based on H_2O_2-containing oxidizing mixtures with reduced acidity; a correlation between the ionization potentials of AF and the oxidative capacity of the mixtures has been found, and a calculated analytical method to determine the choice of oxidizing mixtures has been derived.

Only isolated syntheses of nitro derivatives of furazans (NF) have been described in the broad general literature. At the same time they are of unquestionable interest as prospective energetic materials, physiologically active substances and precursors for various syntheses.[1]

Attempts to introduce the nitro group into the furazan ring by such diverse methods as direct[2,3] and substitutive[3] nitration, as well as diazotization, proved to be unsuccessful. The known NF have been synthesized by oxidation of the appropriate amines.[4–10] Oxidation was hampered because of the low reactivity of the amino group bound to the furazan ring which possesses a considerable electron-accepting effect, similar to that of the dinitrophenyl group.[11] An electron-accepting substituent present in an aminofurazan **1–33a** (AF) renders the amino group still more passive. Thus, early attempts to oxidize 3-amino-4-nitrofurazan,[4,9] even *via* an intermediate sulphilimine derivative,[12] failed. Nevertheless, we felt that the potential of the AF oxidation reaction was far from being exhausted and that conditions for transformation of AF into NF could be found.



1–33a **1–33b**

The clue for effective AF oxidation appeared to us to consist of optimum acidity during the reactions.

The general opinion is that for the oxidizing effect of peroxide oxidizers to be strengthened an increase in concentration and excess of acid is needed. In fact, H_2O_2 solutions in a large excess of concentrated H_2SO_4 were the most effective oxidative mixtures successfully used for the oxidation of such deactivated amines as polynitroanilines.[13] They proved, however, to be unfit for AF oxidation. Reactions with them did not proceed at room temperature, and intense decomposition ensued at an elevated temperature. In the course of investigation we established a very important – and unexpected, from the traditional viewpoint – rule, *viz.* oxidative systems ***with lowered***, not with elevated, ***acid content*** should be used for AF oxidation. Optimum oxidative conditions had, however, to be construed experimentally for each AF separately. The necessity of a general approach to the determination of AF oxidation conditions, involving correlation–calculation methods, has appeared.

For a primary evaluation of reactivity various AF were arranged in a row according to the yield values of NF obtained under the same oxidation conditions. For transition to a calculated scale of reactivity calculated molecular parameters had to be found which would for their part reflect the AF reactivity and also correlate with experimental yield values of NF. To this end we performed quantum chemical calculations (in an MNDO approximation[14] with geometrical parameters fully optimized) of ionization potentials (I), charge values on the nitrogen atoms of the amino group (q_{NH_2}), and the width of the energy gap between higher occupied and lower vacant molecular orbitals (ΔE_{MO}) for AF and their protonated forms. The NF yields were found to correlate only with the ionization potentials of unprotonated AF (I_0). In Table 1 the AF are arranged in the order of increasing I_0, corresponding to a decrease in their capacity to be oxidized to NF. Deviation from this correlation is exhibited by compounds containing a phenyl group in the substituent: they are more inert towards oxidation than could be inferred from their I_0, *e.g.*, compound **4a** ($I_0 = 9.71$ eV) is more difficult to oxidize than compound **14a** ($I_0 = 10.42$ eV). Nevertheless, I_0 could be accepted as an index of the capacity of AF to be oxidized to NF, and using I_0 as a basis a tentative calculated scale of AF reactivity can be constructed.

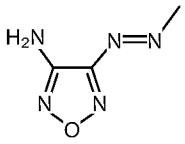
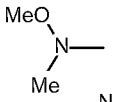
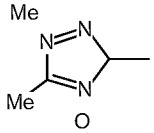
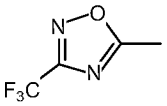
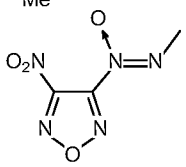
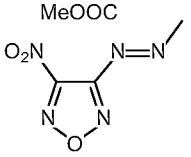
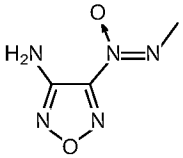
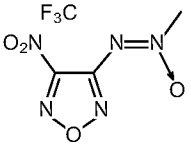
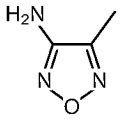
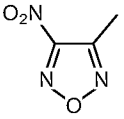
Comparison of I_0 with ionization potentials I_H of protonated AF indicates that protonation renders AF passive, $I_H > I_0$, *e.g.*, for **14a** $I_0 = 10.42$ eV, and $I_H = 15.67$ eV. However, most of the AF shown in Table 1 are protonated just in very acid media.[15] Therefore, an increase in the oxidative activity of H_2O_2/H_2SO_4 mixtures by a traditional increase in H_2SO_4 content should render AF passive and hence be of no use for AF oxidation.

This line of reasoning stresses again the importance of the possibility discovered by us of effectively oxidizing AF in media with reduced H_2SO_4 content. To evaluate the relative activity of these oxidative mixtures and to develop methods for increasing their activity we examined mixtures of H_2O_2 with H_2SO_4, Na_2WO_4 and $(NH_4)_2S_2O_8$. The most active species in these mixtures are H_2SO_5, H_2WO_5 and also some other species of unrevealed structure.[16–18] We suggest that the activity of the oxidative mixtures is determined by the content of these most active species only, not by the general amount of H_2O_2. The concentration of oxidative species is determined by the mole ratio of the mixture of initial components. The most effective mixtures turned out to be those with a mole ratio $H_2O_2/H_2SO_4 > 1$. To evaluate the concentration of the oxidative components of the system and especially that of the most active fraction we have used the thiocyanate method for iodometric titration, proposed by Pungor for the determination of H_2O_2, H_2SO_4 and $H_2S_2O_8$ in their joint presence.[19] The most active fraction we designated arbitrarily by a term "active oxygen" and a symbol [O]. The compositions of the mixtures studied, calculated on the basis of titration data, are shown in Table 2.

Investigation of the oxidation of the amine series listed in Table 1 showed that certain oxidizing mixtures correspond to a fixed ionization potential. The activities [O] of the proper mixtures were set against the ionization potentials I_0 of the corresponding amines. Fig. 1 shows the curve, reflecting the dependence I_0 *versus* [O]. Fig. 1 may also be used to determine the conditions for the oxidation of AFs not shown in Table 1.

The approach adopted by us made it possible to oxidize all

Table 1 Ionization potentials (I_0) of unprotonated AF.

Compound	Aminofurazan (AF) R	I_0/eV	Compound	Aminofurazan (AF) R	I_0/eV
1	PhN=N(O)–	9.57	**17**		10.53
2	PhN=N–	9.62			
3	PhN(O)=N–	9.67			
4	PhO	9.71			
5	Ph	9.79			
6	PhC(O)	9.80			
7	MeO	10.07			
8	H_2N	10.08	**18**	Br	10.54
			19	I	10.55
9		10.18	**20**	HO	10.61
			21	Cl	10.62
			22	MeC(O)	10.65
			23	HOOC	10.73
10		10.31	**24**	F	10.74
			25		10.75
11		10.32	**26**		
			27	NC–	10.83
				MeOOC	10.88
			28		10.89
12		10.35			
			29	Cl_3C	10.91
			30	F_3C	11.05
13	Me_3C	10.41	**31**		11.11
14	Me	10.42			
15		10.44	**32**		11.12
16	H	10.47	**33**	O_2N	11.20

the AF studied to NF† in 75–95% yield; the oxidation was successful even with the most deactivated amine – 3-amino-4-nitrofurazan (**33a**), and 3,4-dinitrofurazan‡ (**33b**) was obtained for the first time.

Further elaboration of the correlation between the oxidative activity of mixtures based on H_2O_2 and AF properties is in progress.

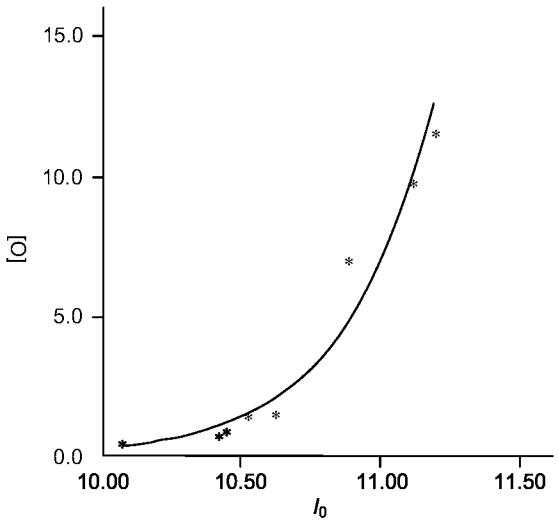


Fig. 1 AF ionization potential *versus* active oxygen content relationship.

† *General procedure for oxidation of AF.* **Caution!** The oxidizing and reaction mixtures, as well as NF themselves, are powerful hazards and should be handled carefully. Sulfuric acid or oleum and, if necessary, Na_2WO_4 or $(NH_4)_2S_2O_8$ referred to in Table 2 were added to H_2O_2 at 0 to −5 °C with stirring and left for 1 h. AF was added to the mixture chosen in accordance with Fig. 1 and stirring was continued at 15–25 °C to completion of the reaction (TLC control) followed by dilution with 2 volumes of water. The product was extracted with CH_2Cl_2 or pentane, then washed with water and dried over $MgSO_4$. The filtrate was stripped of solvent and the residue distilled or recrystallized. If the activity of the oxidizing mixture [O] chosen was somewhat lower than necessary both the formation of NF was slowed down and the yield was decreased; a much reduced [O] for the mixture afforded no AF oxidation. If more [O] was used in the reaction an efficient cooling was required. Still higher [O] values made the reaction mixture decompose vigorously.

The diamines **8a**, **12a**, **15a** and **17a** give the respective aminonitro derivatives, **8b** = **33a**, **12b** = **31a**, **15b** = **32a** and **17b** = **28a**.

‡ Structures of all compounds obtained were proved by elemental analysis, mass, IR and ^1H and ^{13}C NMR spectroscopy. Some selected data, for **33b**: 94% yield, m.p. 15 °C, b.p. 33.5 °C/1 Torr, 168 °C/768 Torr, n_D^{20} 1.4740, ρ_{20} 1.62 g cm^{-3}, IR (ν, cm^{-1}) 1591, 1557, 1460, 1360, 1145, 1040, 849, 812; MS, *m/z*: 160(M^+), 68, 52, 46, 44, 30; ^{13}C NMR (δ, ppm) 153.5. For other compounds (m.p./°C and yield, %): **4b** 94, 83; **5b** 38, 96; **7b** 46, 79; **8b** 125, 78; **12b** 131, 75; **14b** oil, 87; **15b**§ 215, 77; **17b** 93, 75; **20b** 23, 77; **21b** oil, 81; **26b** 18, 94; **32b** 85, 95.

§ This compound was first prepared by T. I. Godovikova and co-workers (N. D. Zelinsky Institute of Organic Chemistry, RAS), unpublished data.

Table 2 Titration data for H_2O_2 oxidizing mixtures.

Entry	Oxidizing mixture (mol ratio of components)	Active oxygen content by titration data, mol dm^{-3} [O]
1	H_2O_2 [a]/H_2SO_4(1:1)	0.42
2	H_2O_2 [a]/H_2SO_4(2:1)	0.45
3	H_2O_2 [a]/oleum [b](2:1)	0.73
4	H_2O_2 [a]/oleum [b](1:1)	0.78
5	H_2O_2 [c]/H_2SO_4(2:1)	0.87
6	H_2O_2 [c]/H_2SO_4(1:1)	1.05
7	H_2O_2 [a]/H_2SO_4/Na_2WO_4 (2:1:0.05)	1.50
8	H_2O_2 [a]/H_2SO_4/Na_2WO_4 (1:1:0.05)	1.64
9	H_2O_2 [a]/H_2SO_4/$(NH_4)_2S_2O_8$ (2:1:0.5)	2.24
10	H_2O_2 [d]/H_2SO_4(1:6)	2.62
11	H_2O_2 [e]/H_2SO_4(2:1)	2.91
12	H_2O_2 [a]/H_2SO_4/$(NH_4)_2S_2O_8$ (2:1:1)	5.56
13	H_2O_2 [e]/H_2SO_4(1:1)	7.14
14	H_2O_2 [d]/H_2SO_4(1:1)	9.81
15	H_2O_2 [d]/H_2SO_4(2:1)	9.82
16	H_2O_2 [d]/H_2SO_4/Na_2WO_4 (2:1:0.05)	11.74

[a] Using 30% H_2O_2. [b] 26% oleum. [c] 50% H_2O_2. [d] 93% H_2O_2. [e] 77% H_2O_2.

References

1 J. H. Boyer, *Nitroazoles*, Deerfield Beach, Florida: VCN, 1986, 341.
2 A. De Munno, V. Bertini, A. Menconi and G. Denti, *Atti Soc. Tosc. Sci. Nat., Mem., Serie A*, 1974, **81**, 334.
3 M. P. Zelenov, G. M. Frolova, S. F. Melnikova and I. V. Tselinskii, *Khim. Geterotsikl. Soedin.*, 1982, 27 [*Chem. Heterocycl. Compd. (Engl. Transl.)*, 1982, 21].
4 M. D. Coburn, *J. Heterocycl. Chem.*, 1968, **5**, 83.
5 R. Calvino, V. Mortarini, A. Gasco, A. Sanfilippo and M. L. Ricciardi, *Eur. J. Med. Chem.-Chim. Therap.*, 1980, **15**, 485.
6 N. N. Makhova, I. V. Ovchinnikov, B. N. Khasapov and L. I. Khmelnitskii, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1982, 646 (*Bull. Acad. Sci. USSR, Div. Chem. Sci.*, 1982, 573).
7 G. D. Solodyuk, M. D. Boldyrev, B. V. Gidaspov and V. D. Nikolaev, *Zh. Org. Khim.*, 1981, **17**, 861 [*J. Org. Chem. USSR (Engl. Transl.)*, 1981, **17**, 756].
8 M. D. Coburn, *J. Heterocycl. Chem.*, 1986, **23**, 421.
9 A. B. Sheremetev, T. S. Novikova, T. M. Melnikova and L. I. Khmelnitskii, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1990, 1193 (*Bull. Acad. Sci. USSR, Div. Chem. Sci.*, 1990, 1073).
10 A. B. Sheremetev and O. V. Kharitonova, *Mendeleev Commun.*, 1992, 157.
11 L. I. Khmelnitskii, S. S. Novikov and T. I. Godovikova, *Khimiya Furoksanov: Stroenie i Sintez (Chemistry of Furoxans: Structure and Synthesis)*, Nauka, Moscow, 1981, p. 215.
12 M. C. Coburn, B. W. Harris, K.-Y. Lee, M. M. Stinecipher and H. H. Hayder, *Ind. Eng. Chem., Prod. Res. Dev.*, 1986, **25**, 68.
13 A. T. Nielsen, R. L. Atkins, W. P. Norris, C. L. Coon and M. E. Sitzmann, *J. Org. Chem.*, 1980, **45**, 2341.
14 T. Clark, *A Handbook of Computational Chemistry*, John Wiley & Sons, New York, 1987.
15 I. V. Tselinskii, S. F. Melnikova and S. V. Vergizov, *Khim. Geterotsikl. Soedin.*, 1981, 321 [*Chem. Heterocycl. Compd. (Engl. Transl.)*, 1981, 228].
16 D. I. Metelitsa, *Usp. Khim.*, 1972, **41**, 1737 (*Russ. Chem. Rev.*, 1972, **41**, 807).
17 M. Hedayatullah, *Bull. Soc. Chim. Fr.*, 1972, **7**, 2966.
18 K. Kahr and C. Berther, *Chem. Ber.*, 1960, **93**, 132.
19 E. Pungor, E. Schulek and J. Trompler, *Acta Chim. Acad. Sci. Hung.*, 1954, **4**, 423.

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